DETAILED ACTION

The preliminary amendment filed on 5 May 2005 in which claims 1-59 were cancelled, and claims 60-80 are newly added, is acknowledged.

Claims 60-80 are pending in the instant application.

Priority

This application is a National Stage entry of PCT/FI03/00840 filed on 6 November 2003 and claims priority to Finland foreign application 20021989 filed on 6 November 2002. Applicants are requested to note that contrary to what was indicated in the previous Office Action dated 15 July 2008, the certified copy of the foreign priority document received in the Office is in English.

Information Disclosure Statement

The information disclosure statement filed 5 May 2005 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered, except for the U.S. Patent document.

Election/Restrictions

Applicant's election with traverse of Group III, claims 71 and 72, drawn to a method of treating a condition due to the presence of *Helicobacter pylori*, in the reply filed on 14 January 2009 is acknowledged. The Applicant further elects the species NeuNAcα3Galβ4GlcNAcβ3Gal in response to the requirement for the election of a single disclosed species. The traversal is on the ground(s) that insufficient reasoning was set forth for the restriction, that the restriction is improper and should at most be subject to a species election rather than a restriction, and that it would not be an undue burden to examine the claims as presented. The Applicants argue that the common technical feature in all groups is the binding of *H. pylori* to the substances as defined in claim 60 or 68, and that this new binding phenomena is not disclosed in the prior art. The Applicants further argue that although Mollicone *et al.* may teach related subject matter of the product claim 60, the document does not disclose any pharmaceutical or nutritional composition comprising any of the substances of claim 60.

These arguments are not found persuasive because, according to PCT Rule 13.1, unity of invention exists only when there is a technical relationship among the claimed inventions involving one or more of the same or corresponding special technical features. As defined in PCT Rule 13.2, the expression "special technical features" means those technical features that define a contribution which each of the inventions, considered as a whole, makes over the prior art. As indicated in the Office Action dated 15 July 2008, the common technical feature in all groups is the LacNAcβ3Gal structure and that the structure is disclosed by Mollicone *et al.*

Although Applicants argue that the common technical feature in all groups is the binding of *H. pylori* to the substances as defined in claim 60 or 68, and that the Mollicone *et al.* reference does not disclose any pharmaceutical or nutritional composition comprising any of the substances of claim 60, claim 80 makes no recitations to those effects. Instant claim 80 does not specify that the compounds are pharmaceutical or nutritional compositions, nor does the claim indicate that the compounds bind to *H. pylori*. As a result, these aspects are not considered a common technical feature of the inventions.

Upon further evaluation of the claims, it is considered that the common technical feature in all the groups is the NeuNAcα3LacNAcβ3Gal structure, rather than the LacNAcβ3Gal structure as indicated in the Office Action dated 15 July 2008. Thus, the prior art of Teneberg *et al.* (PTO-892, Ref. V) is currently applied to show that this common technical feature fails to make a contribution over the prior art with respect to novelty and inventive step. Teneberg *et al.* disclose that the minimal oligosaccharide epitope required for binding of the neutrophil-activating protein of *H. pylori* is a terminal linear NeuAcα3Galβ4GlcNAcβ3Galβ or NeuAcα3Galβ4GlcNAcβ3Galβ4GlcNAcβ sequence (p. 19070, column 1, first full paragraph). Furthermore, carbohydrate analogs of these proposed binding-active sequences were synthesized for inhibition studies (p. 19071, column 1, last paragraph). For the reasons indicated above and in view of the applied Teneberg *et al.* reference, the inventions lack unity, and therefore, restriction for examination purposes as indicated is proper.

The requirement is still deemed proper and is therefore made FINAL.

Claims 60-70 and 73-80 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 14 January 2009.

Claims 71 and 72 will be examined on its merits herein.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 71 and 72 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation "pharmaceutically effective amount" in claim 71 renders the claims herein indefinite. In the absence of further guidance in the specification, it is unclear what amount constitutes a "pharmaceutically effective amount". Thus, one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

The recitation "a condition due to the presence of *Helicobacter pylori*" in claim 71 renders the claims herein indefinite. It is noted that Applicants provide examples of conditions due to the presence of *Helicobacter pylori* that are treatable according to the invention on p. 33 of the instant specification. However, these examples are not viewed to be limiting. Thus, one of ordinary skill in the art would not be reasonably apprised of

the scope of the invention. It is respectfully suggested that Applicants incorporate the specific conditions into the claim to render the claim definite with respect to what condition the Applicants are intending to treat.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Written Description

Claims 71 and 72 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims are directed to a method for the treatment of a condition due to the presence of *Helicobacter pylori* wherein a pharmaceutically effective amount of the substance as defined in claim 60 is administered to a subject in need of such a treatment.

The claims are rejected under the written description requirement for failing to disclose any specific examples for the treatment of a condition due to the presence of *Helicobacter pylori* in a patient by administering a pharmaceutically effective amount of

the substance as defined in claim 60, so as to sufficiently show the Applicant was in possession of the claimed subject matter.

The Guidelines for Examination of Patent Applications under the 35 USC § 112, first paragraph, "Written Description" Requirement", published at Federal Register, Vol. 66, No. 4, pp. 1099-1111 outline the method of analysis of claims to determine whether adequate written description is present. The first step is to determine what the claim as a whole covers, i.e., discussion of the full scope of the claim. Second, the application should be fully reviewed to understand how applicant provides support for the claimed invention including each element and/or step, i.e., compare the scope of the claim with the scope of the description. Third, determine whether the applicant was in possession of the claimed invention as a whole at the time of filing. This should include the following considerations: (1) actual reduction to practice, (2) disclosure of drawings or structural chemical formulas, (3) sufficient relevant identifying characteristics such as complete structure, partial structure, physical and/or chemical properties and functional characteristics when coupled with a known or disclosed correlation between function and structure, (4) method of making the claimed invention, (5) level of skill and knowledge in the art and (6) predictability of the art.

For claims 71 and 72, each of these factors has been considered, with the most relevant factors discussed below. For each claim drawn to a genus, each of these factors is to be considered to determine whether there is disclosure of a representative number of species that would lead one skilled in the art to conclude that applicant was in possession of the claimed invention. Where skill and knowledge in the art is high,

adequate written description would require fewer species to be disclosed than in an art where little is known; further, more species would need to be disclosed to provide adequate written description for a highly variable genus.

First, what do the claims as a whole cover? Claim 71 and dependent therefrom, are directed to a method for the treatment of a condition due to the presence of *Helicobacter pylori* wherein a pharmaceutically effective amount of any substance as defined in claim 60 is administered to a subject in need of such a treatment.

Second, how does the scope of the claims compare to the scope of the disclosure? The method claimed is broader than what is supported in the disclosure. The only disclosure for the claimed method is the statement that "it is *possible* to incorporate the *Helicobacter pylori* binding substance, optionally with a carrier, in a pharmaceutical composition, which is suitable for the treatment of a condition due to the presence of *Helicobacter pylori* in a patient or to use the *Helicobacter pylori* binding substance in a method for treatment of such conditions" (emphasis added) (p. 33 of the instant specification, lines 22-33).

Third, the factors need to be considered, with the most relevant factors discussed below.

Reduction to Practice: The Specification fails to disclose any evidence, other than theory, to suggest that the instantly claimed method has successfully treated patients with a condition due to the presence of *Helicobacter pylori*. There is no evidence presented to support the claimed methods of treatment.

Sufficient Relevant Identifying Characteristics: The disclosure only discloses one specific binding substance of claim 60, namely a pentasaccharide (p. 49, lines 11-19), in the form of free oligosaccharide or linked to a hexadecylaniline aglycone (p. 51, lines 1-9). Additionally, other specific binding substances are disclosed that are bound to ceramide, although these compounds fall outside the scope of the instant claims. Furthermore, there is no disclosure for an effective dosage of the disclosed binding substances of claim 60 for administration in the instantly claimed method.

Level of Skill in the Art and Knowledge in the Art: The level of skill in the art is high, about that of a Ph.D scientist with several years of experience.

Thus, having analyzed the claims with regard to the Written Description guidelines, it is clear that the specification does not disclose sufficient information in support for the method of treating a patient with a condition due to the presence of *Helicobacter pylori* by administering an effective dosage of a binding substance of claim 60. Thus, in the absence of any working examples or evidence in the specification supporting the *possibility* that the methods can be used successfully, one skilled in the art would be lead to conclude that Applicant was not in possession of the claimed invention.

Scope of Enablement

Claims 71 and 72 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of specific conditions due to the presence of *Helicobacter pylori* using specific compounds of claim 60, does not

reasonably provide enablement for the treatment of any condition due to the presence of *Helicobacter pylori* using any compound of claim 60, or for the prevention of any condition due to the presence of *Helicobacter pylori*. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

As indicated on p. 34 of the instant Specification, the term "treatment" relates to "treatment in order to cure of alleviate a disease or a condition," as well as "treatment in order to prevent the development of a disease or condition." No limiting definition of "to prevent" is given in the specification. In the absence of a limiting definition by the applicant, prevent, as described according the Merriam-Webster online dictionary (PTO-892, Ref. U), is to keep from happening or existing. Thus the claimed method capable of preventing a condition due to the presence of *Helicobacter pylori* is interpreted to be an amount with which a skilled practitioner of the medical or pharmaceutical arts would be capable of completely eliminating the occurrence of a condition due to the presence of *Helicobacter pylori*, by administering any substance as defined in claim 60 to the subject before the onset of the condition.

Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or

guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

All of the *Wands* factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the invention: The rejected invention is drawn to a method for the treatment of any condition due to the presence of *Helicobacter pylori* using any compound of claim 60, and for the prevention of any condition due to the presence of *Helicobacter pylori*.

Relative skill of those in the art: The relative skill of those in the art is high.

Breadth of claims: The claims specifically include any compound of formula (1) of claim 60, any condition due to the presence of *Helicobacter pylori*, and the prevention any condition due to the presence of *Helicobacter pylori*.

State of the prior art/Predictability or unpredictability of the art: The skilled artisan would view that the treatment to prevent any condition due to the presence of *Helicobacter pylori* totally or absolutely, or not even occurring for the first time, is highly unlikely. Furthermore, as indicated by Teneberg *et al.* (PTO-892, Ref. V), "the pathogenesis of *H. pylori*-induced gastroduodenal diseases is likely to be a complex process, and no single event or phenomenon may be solely responsible for all its clinical manifestations" (p. 19071, column 1, third full paragraph). Thus, it is unlikely that the compounds (binding substances) used in the method of treatment, which bind to the *H. pylori* neutrophil-activating protein glycolipid receptor, is sufficient in

themselves to even treat all known conditions due to the presence of *H. pylori*, let alone a method of preventing the condition from occurring.

Amount of guidance/Existence of working examples: Other than suggesting that "it is *possible* to ... use the *Helicobacter pylori* binding substance in a method for treatment of such conditions" (emphasis added) (p. 33 of the instant specification, lines 22-33), there are **no** working examples present to indicate that the proposed theory is in fact successful.

Lack of a working example is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art. See MPEP 2164.

Quantity of experimentation necessary: In order to practice the invention with the full range of all possible treatment conditions due to the presence of *Helicobacter pylori* beyond those known in the art, as well as all possible treatment methods beyond those known in the art, such as using any binding substance of claim 60 in a method to prevent any and all conditions due to the presence of *Helicobacter pylori*, one skilled in the art would need to undertake a novel and extensive research program to show that the binding substance of claim 60 prevented any and all conditions due to the presence of *Helicobacter pylori* from occurring. Because this research would have to be exhaustive, and because it would involve such a wide and unpredictable scope of use, it would constitute an undue and unpredictable experimental burden. Furthermore, as there is no disclosure of any dosage guideline or of pharmaceutically effective amount in any examples, a skilled artisan would need extensive experimentation to practice the

invention as instantly claimed (*Impax Laboratories, Inc. v. Aventis Pharmaceuticals Inc.*, No. 07-1513, Fed. Cir. Oct. 3, 2008).

Thus, the specification fails to provide clear and convincing evidence in sufficient support for the treatment of any condition due to the presence of *Helicobacter pylori* using any compound of claim 60, or for the prevention of any condition due to the presence of *Helicobacter pylori*, as recited in the instant claims.

Genetech, 108 F.3d at 1366, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the *Wands* factors as discussed above, e.g., the amount of guidance provided, the predictability of the art and the lack of working examples, Applicants fail to provide information sufficient to practice the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 71 and 72 are rejected under 35 U.S.C. 103(a) as being unpatentable over WIPO publication WO 02/056893 to Miller-Podraza *et al.* (PTO-892, Ref. N) in view of journal publication by Teneberg *et al.* (PTO-892, Ref. V).

Miller-Podraza *et al.* teach a substance or a receptor comprising a *Helicobacter pylori* binding oligosaccharide sequence and its use in pharmaceutical and nutritional compositions for the treatment of conditions due to the presence of *Helicobacter pylori* (p. 1, lines 5-9). The *Helicobacter pylori* binding substance has the formula

$[Gal(A)_q(NAc)_r/Glc(A)_q(NAc)_r\alpha 3/\beta 3]_s[Gal\beta 4GlcNAc\beta 3]_tGal\beta 4Glc(NAc)_u$ wherein q, r, s, t, and u are each independently 0 or 1 (p. 2, lines 24-35). The *Helicobacter pylori* binding sequences can be part of a natural or synthetic glycoconjugate or a free oligosaccharide or part of a free oligosaccharide (p. 12, lines 21-23). The *Helicobacter pylori* binding substance can also comprise a mix of the *Helicobacter pylori* binding oligosaccharide sequences (p. 12, lines 31-32). Among a list of *Helicobacter pylori* binding substances include Galβ4GlcNAc and Galβ4GlcNAcβ3Galβ4GlcNAc (p. 16, lines 21-35). Furthermore, it is known that *Helicobacter pylori* can bind several kinds of oligosaccharide sequences (p. 21, lines 24-25). The *Helicobacter pylori* binding substance, optionally with a carrier, can be incorporated in a pharmaceutical composition for the treatment of conditions due to the presence of *Helicobacter pylori* (p. 22, lines 4-8). Examples of treatable conditions include chronic superficial gastritis, gastric ulcer, duodenal ulcer, non-Hodgkin lymphoma in human stomach, gastric adenocarcinoma, among others (p. 22, lines 8-14). Additionally, Miller-Podraza *et al.* teach that the *Helicobacter pylori* binding substance can be used as part of a nutritional composition including food- and feedstuff, preferably as part of a functional food (p. 23, lines 15-18). The functional food has a positive effect on one's health by inhibiting the binding of *Helicobacter pylori* to target cells or tissues (p. 23, lines 18-20).

Miller-Podraza *et al.* do not disclose a *Helicobacter pylori* binding substance that also includes a terminal sialic acid residue.

Teneberg *et al.* teach that the minimal oligosaccharide epitope required for binding of the neutrophil-activating protein of *H. pylori* is a terminal linear

NeuAcα3Galβ4GlcNAcβ3Galβ or NeuAcα3Galβ4GlcNAcβ3Galβ4GlcNAcβ sequence (p. 19070, column 1, first full paragraph). A prominent feature of *H. pylori*-induced gastritis is infiltration of the gastric lamina propria by neutrophil granulocytes, and neutrophils are also seen permeating between the epithelial cells (p. 19067, column 1, second paragraph). The neutrophil-activating protein induces an increased expression of CD11b/Cd18 on neutrophils and promotes the adhesion of neutrophils to endothelial cells (p. 19067, column 2, bridging paragraph). Preliminary results by Tenebert *et al.* of initial inhibition studies indicate that phagocytosis of the neutrophil-activating protein by preactivated human neutrophils may be partly inhibited by the synthetic carbohydrate analogs of the proposed binding-active sequence (p. 19071, column 1, last paragraph).

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Miller-Podraza *et al.*, concerning methods for the treatment of conditions due to the presence of *Helicobacter pylori* comprising *Helicobacter pylori* binding substances as a pharmaceutical or nutritional composition, with the teachings of Teneberg *et al.*, regarding NeuAcα3Galβ4GlcNAcβ3Galβ or NeuAcα3Galβ4GlcNAcβ3Galβ4GlcNAcβ as the minimal oligosaccharide epitope required for binding of the neutrophil-activating protein of *H. pylori*. Since Miller-Podraza *et al.* teach that *Helicobacter pylori* can bind several kinds of oligosaccharide sequences and Teneberg *et al.* teach that two such sequences are NeuAcα3Galβ4GlcNAcβ3Galβ and NeuAcα3Galβ4GlcNAcβ3Galβ4GlcNAcβ, one would have been motivated to combine the teachings in an effort to inhibit all possible binding sites of *H. pylori*.

Thus, the claimed invention as a whole is *prima facie* obvious over the combined teachings of the prior art.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SCARLETT GOON whose telephone number is 571-270-5241. The examiner can normally be reached on Mon - Thu 7:00 am - 4 pm and every other Fri 7:00 am - 12 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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